Lynch Syndrome Screening Network

# *The Lynch Syndrome Screening Network: Promoting Universal Screening for Newly Diagnosed Colorectal Cancers in Michigan and the Nation*

Karmanos Cancer Institute
March 23, 2015

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Genomics Coordinator
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# *Learning Objectives*

- State the Healthy People 2020 objective regarding Lynch syndrome and the importance of the EGAPP evidence-based recommendation
- Name three ways that Michigan is working to increase awareness of the EGAPP recommendation for Lynch syndrome
- Describe the Lynch Syndrome Screening Network (LSSN) as a resource for health systems to implement universal screening for Lynch syndrome on newly diagnosed colorectal cancers

# *Governor Snyder Proclaims Lynch Syndrome Hereditary Cancer Awareness Week as March 22nd-March 28th*


STATE OF MICHIGAN

CERTIFICATE OF PROCLAMATION

ON BEHALF OF THE PEOPLE OF MICHIGAN

I, Rick Snyder, governor of Michigan, do hereby proclaim

March 22 - 28, 2015

LYNCH SYNDROME HEREDITARY CANCER AWARENESS WEEK

WHEREAS, Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC), is an inherited disorder associated with higher risks of developing colorectal, endometrial, pancreatic, ovarian, urinary tract, and other types of cancer; and,

WHEREAS, it is estimated that one in every 400 Americans have Lynch syndrome and of those, have up to an 80 percent risk of developing colorectal cancer, and that their first-degree relatives have a 50 percent risk of having the disorder as well; and,

WHEREAS, only five percent of those with a personal or family history of colon cancer have been screened for Lynch syndrome; and,

WHEREAS, the Centers for Disease Control and Prevention (CDC) recommends Lynch syndrome screening for all patients newly diagnosed with colorectal cancer, regardless of age and family or personal history, in order to identify whether they have the condition; and,

WHEREAS, cascade screening identifies at-risk relatives of individuals with Lynch syndrome, and is an important measure toward preventing cancer in those at-risk family members; and,

WHEREAS, every person should discuss their health history with their health care provider to assess their risk for hereditary cancers; and,

WHEREAS, screening and diagnosis of Lynch syndrome, whether personal or in the family, can improve cancer prevention and treatment; and,

WHEREAS, on this day, we join with the Michigan Department of Community Health and public health partners to raise awareness of Lynch syndrome in Michigan; we encourage all residents to learn more about this hereditary disorder, to gather their family health history, and to take appropriate steps toward cancer risk assessment, detection and prevention;

NOW, THEREFORE, I, Rick Snyder, governor of Michigan, do hereby proclaim March 22-28, 2015 as Lynch Syndrome Hereditary Cancer Awareness Week in Michigan.

Rick Snyder
Governor

Michigan Cancer Genetics Alliance Membership Meeting
March 20, 2015

# *Examples of MDCH Promotion of Governor's Proclamation*

- Michigan Cancer Genetics Alliance (MCGA) celebrated on March 20th; photo taken and posted to Lynch Syndrome International (LSI); LSI promotional materials disseminated to MCGA members
  - Anyone can become member of MCGA
  - Contact duquetted@michigan.gov to join
  - Banner to promote universal screening for Lynch syndrome
- Michigan Department of Community Health (MDCH) to release news of Lynch Syndrome Hereditary Cancer Awareness Week through press release
- Post a variety of Lynch syndrome informational messages to MDCH Facebook and MDCH Twitter
- Partner with LSI, MCGA, CDC, and others to increase awareness

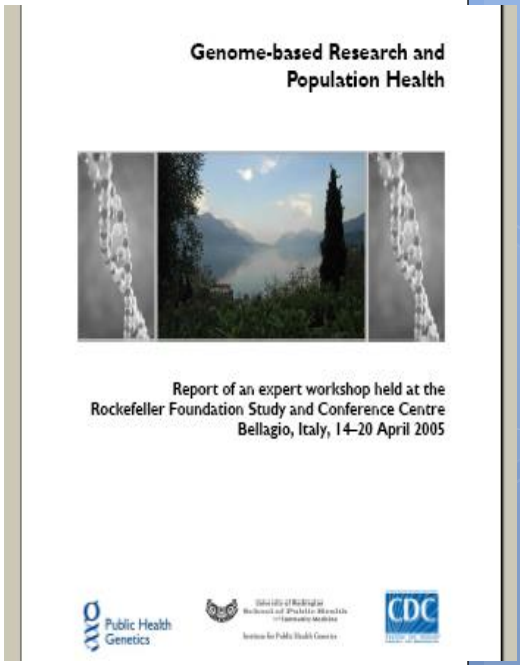
# *Genomics and Public Health in the 21st Century*

"Genomics will be to the 21st century what infectious disease was to the 20th century…Genomics should be considered in every facet of public health: infectious disease, chronic disease, occupational health, environmental health, in addition to maternal and child health"

Gerard et al. Journal Law, Medicine , Ethics 2002; vol 30(suppl):173-176

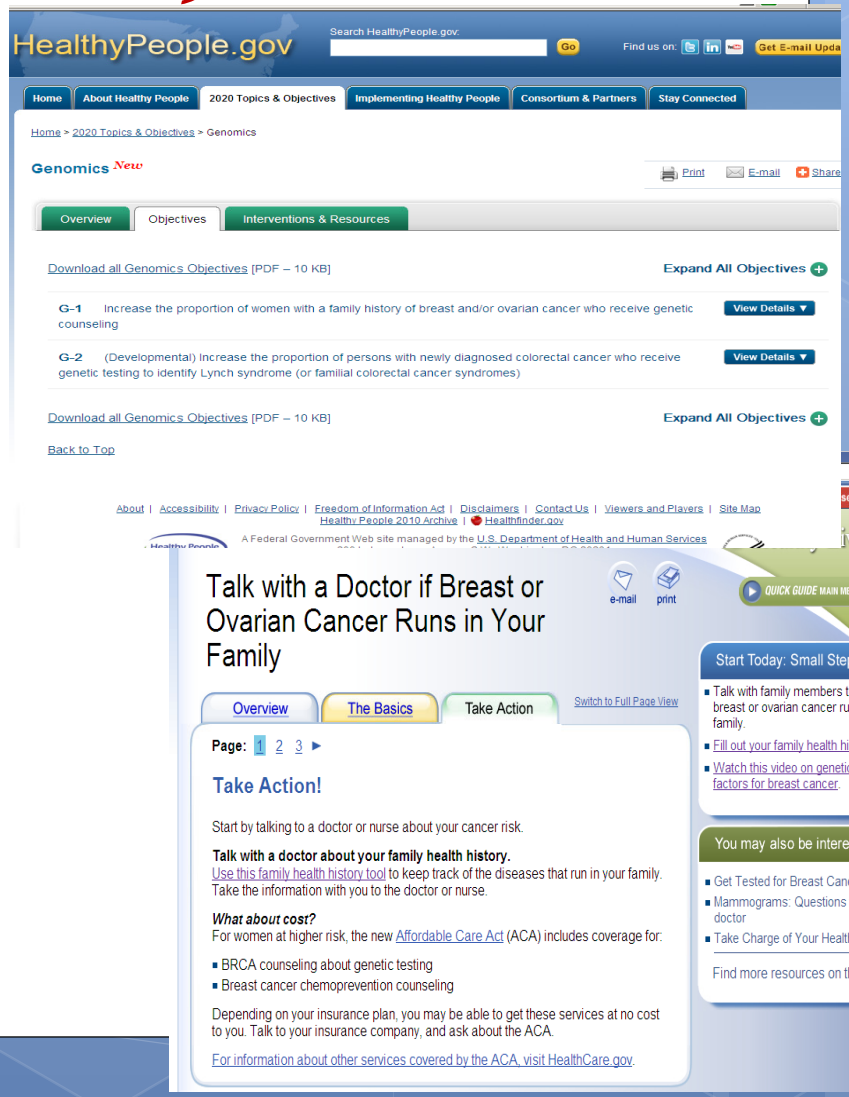
# *What is "Public Health Genomics"? (Bellagio Statement, 2006)*

"A multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health."



# Healthy People 2020 (HP 2020)

- Started in 1979
- 10-year national objectives for promoting health and preventing disease
- **HP 2020 marks first time for genomics objectives**
- Encourage collaborations across sectors, guide individuals toward making informed health decisions, and measure the impact of prevention activities
- Works to achieve increased quality and years of healthy life and the elimination of health disparities.

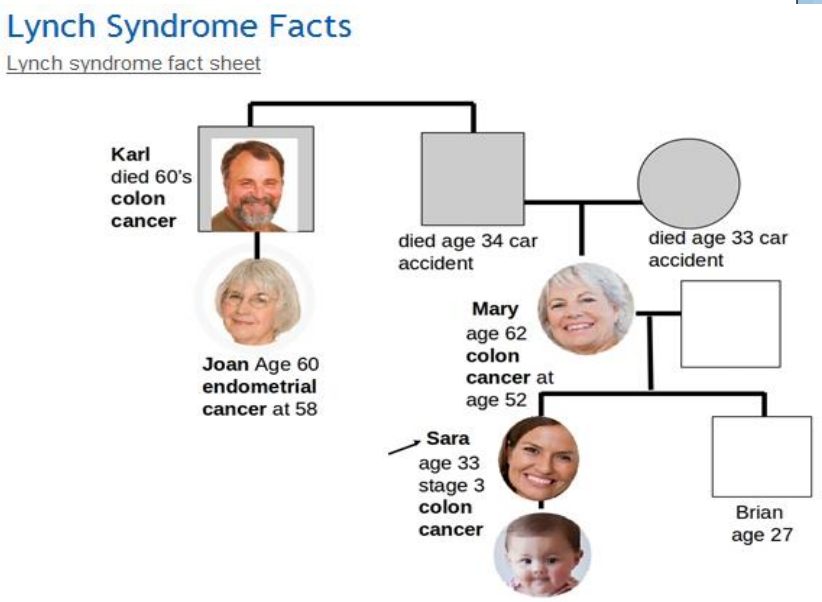


# *Healthy People 2020 Approved Genomics Objective (Developmental)*

"Increase the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome"

# *What is Lynch Syndrome (LS)?*

- Autosomal dominant hereditary cancer syndrome
  - Most common hereditary colorectal (CRC) and uterine cancer syndrome
    - 20-80% lifetime risk for CRC cancer
  - Increased risk of endometrial, ovarian, urinary tract, gastric tract, small bowel, pancreas, sebaceous cancers
  - Due to mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM genes
    - Risk varies based on specific mutation



National Comprehensive Cancer Network®

# NCCN Guidelines Version 2.2014
# Lynch Syndrome

NCCN Guidelines Index
Colon Genetics TOC
Discussion

**Cancer Risk Up to Age 70 Years in Individuals with Lynch Syndrome Compared to the General Population**

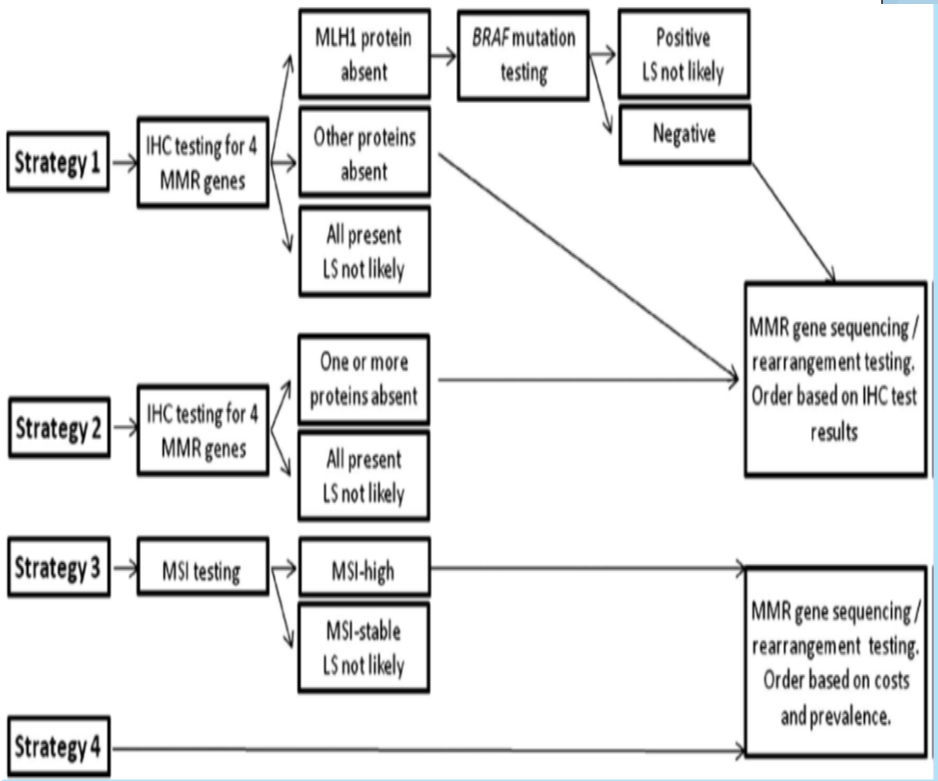
| Cancer | General Population Risk[1] | *MLH1* and *MSH2*[1,2] | | *MSH6*[2] | | *PMS2*[3] | |
|---|---|---|---|---|---|---|---|
| | | Risk | Mean Age of Onset | Risk | Mean Age of Onset | Risk | Mean Age of Onset |
| Colon | 5.5% | 40%-80% | 44-61 years | 10%-22% | 54 years | 15%-20% | 61-66 years |
| Endometrium | 2.7% | 25%-60% | 48-62 years | 16%-26% | 55 years | 15% | 49 years |
| Stomach | <1% | 1%-13% | 56 years | ≤3% | 63 years | † | 70-78 years |
| Ovary | 1.6% | 4%-24%[5] | 42.5 years | 1%-11% | 46 years | † | 42 years |
| Hepatobiliary tract | <1% | 1.4%-4% | 50-57 years | Not reported | Not reported | † | Not reported |
| Urinary tract | <1% | 1%-4% | 54-60 years | <1% | 65 years | † | Not reported |
| Small bowel | <1% | 3%-6% | 47-49 years | Not reported | 54 years | † | 59 years |
| Brain/CNS | <1% | 1%-3% | ~50 years | Not reported | Not reported | † | 45 years |
| Sebaceous neoplasms | <1% | 1%-9% | Not reported | Not reported | Not reported | Not reported | Not reported |
| Pancreas[4] | <1% | 1%-6% | Not reported | Not reported | Not reported | Not reported | Not reported |

[1]Adapted from Kohlmann W, Gruber SB (Updated September 20, 2012) Lynch Syndrome. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1993-2014. Available at http://www.genetests.org. Accessed February 21, 2014.
[2]Bonadona V, Bonaïti B, Olschwang S, et al. French Cancer Genetics Network. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. JAMA 2011;305:2304-2310.
[3]Senter L, Clendenning M, Sotamaa K, et al. The clinical phenotype of Lynch syndrome due to germ-line PMS2 mutations. Gastroenterology 2008;135:419-428.
[4]Kastrinos F, Mukherjee B, Tayob N, et al. Risk of pancreatic cancer in families with Lynch syndrome. JAMA 2009;302:1790-1795.
[5]The 24% risk reported in Bonadona V et al. (JAMA 2011;305:2304-2310) included wide confidence intervals (1%-65% for MLH1; 3%-52% for MSH2).
†The combined risk for renal pelvic, stomach, ovary, small bowel, ureter, and brain is 6% to age 70 (Senter L, et al. Gastroenterology 2008;135:419-428).

**Note: All recommendations are category 2A unless otherwise indicated.**
**Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.**

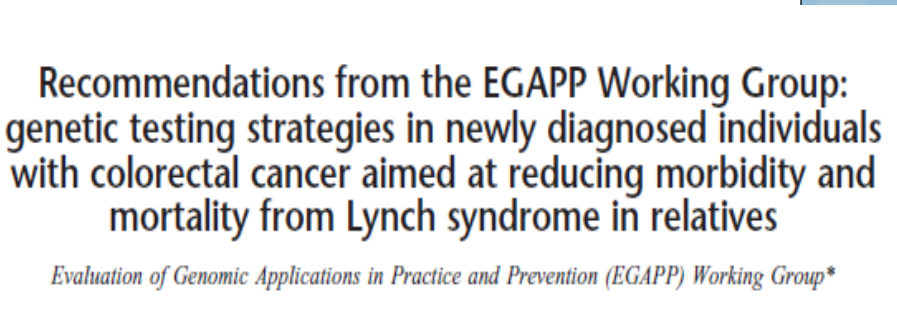
# Lynch Syndrome

- Screening is complex!
  - Bethesda and Amsterdam criteria
  - Multiple approaches including IHC and/or MSI testing on tumor with DNA testing
  - Different genes involved in LS
    - MSH2, MSH6, MLH1, PMS2, EPCAM
- Cancer surveillance & prophylactic survey options
  - Colonoscopy every 1-2 years beginning at ~20-25 years old or 10 years earlier that youngest case in family
  - Annual endometrial sampling and transvaginal ultrasound beginning at 30 years old
  - History and exam annually begin at 21 years
  - Annual urinalysis
  - Prophylactic surgery including subtotal colectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy



# Evaluation of Genomic Applications in Practice and Prevention (EGAPP)

- Launched by CDC in 2004
- Aims:
  - Establish systematic evidence-based process for assessing genetic tests and genetic technology in transition from research to clinical and public health practice
- Process:
  - Develop process for evaluation
  - Independent multidisciplinary workgroup of non-federal experts to develop methods, make recommendations
  - Steering Committee of federal agencies
  - Stakeholder Group for consultation, evaluation


Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives

*Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group**

http://egappreviews.org

# *EGAPP Lynch Recommendation*

## Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives

GIM, 2009;1:35

*Evidence Report/Technology Assessment*
Number 150

**Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications**

May, 2007
www.ahrq.gov/downloads/pub/evidence/pdf/hnpcc/hnpcc.pdf

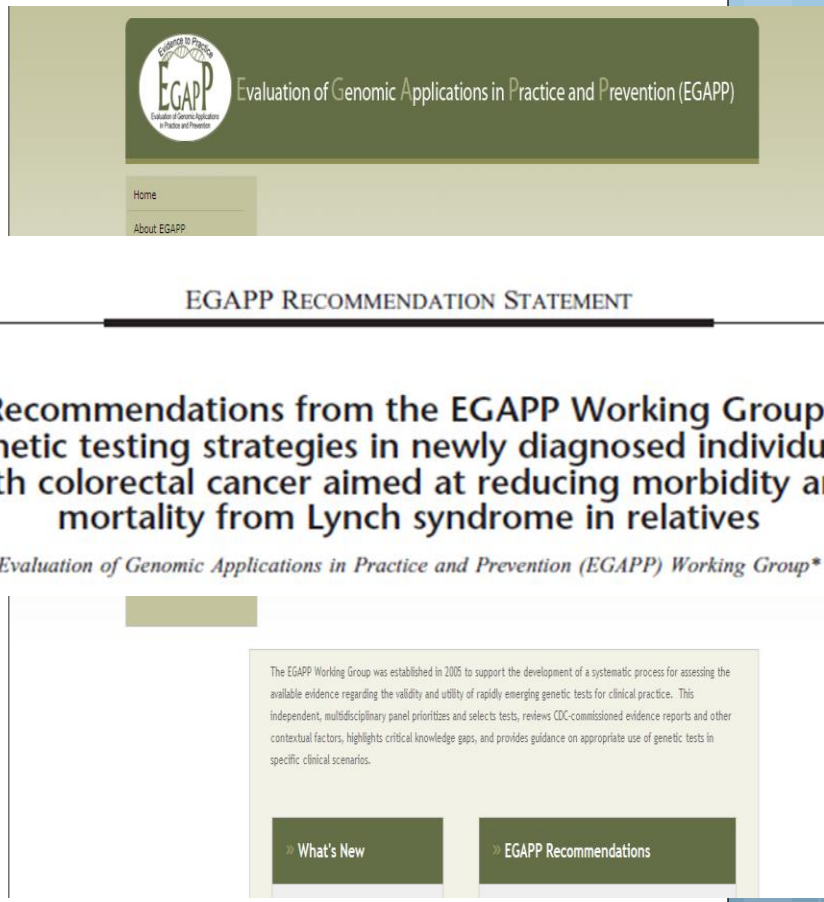
EVIDENCE REVIEW

**EGAPP supplementary evidence review: DNA testing strategies aimed at reducing morbidity and mortality from Lynch syndrome**

GIM, 2009;1:42

# *EGAPP Recommendation on Genetic Testing for Lynch Syndrome*

- Sufficient evidence to offer counseling & genetic testing for Lynch syndrome to patients newly diagnosed with colorectal cancer to reduce morbidity & mortality in relatives
- Relatives of patients who test positive for Lynch could be offered counseling, testing &, if positive, increased colonoscopy
- Evidence of benefit to the patient's relatives




*Gen Med* 2009;11:35-41&42-65

- "…***efforts are needed not only to implement what is known in genomics to improve health but also to reduce potential harm and create the infrastructure needed to derive health benefits in the future.***"

  – Khoury M et al. Am J Prev Med 2011; 40(4):486-493

# *Three-Tier Classification of Recommendations on Genomic Applications*

- **Tier 1: Ready for implementation**
  - Demonstrated analytic validity, clinical validity, clinical utility and evidence-based recommendations
  - Health professionals:  encourage use; can save lives!
    - Examples: ***BRCA (Grade B),*** **Lynch syndrome, familial hypercholesterolemia**, newborn screening

- **Tier 2: Informed decision making**
  - Adequate information on analytic and clinical validity, promising but not definitive information on clinical utility; no evidence-based guidelines recommending clinical use
  - Health professionals: provide information for shared decision making
    - Examples: Gene expression profiles in breast cancer, family history assessment in primary care

- **Tier 3: Discourage use**
  - No or little information on analytic, clinical validity or clinical utility; or evidence of harm
  - Health professionals: discourage use; may be considered for research in select instances; reduce potential harms and save unnecessary healthcare costs
    - Examples:  ***BRCA (Grade D),*** Population screening for hereditary hemochromatosis, personal genomic tests sold directly to consumers

Khoury MJ et al. Am J Prev Med 2011;
Bowen MS et al Public Health Genomics 2012

# *Three-Tier Classification*

**Green**

- FDA label requires use of test to inform choice or dose of a drug
- CMS covers testing
- Clinical practice guidelines based on systematic review supports testing

**Yellow**

- FDA label mentiones biomarkers*
- CMS coverage with evidence development
- Clinical practice guideline, not based on systematic review, supports use of test
- Clinical practice guideline finds insufficient evidence but does not discourage use of test
- Systematic review, without clinical practice guideline, supports use of test
- Systematic review finds insufficient evidence but does not discourage use of test
- Clincial practice guideline recommends dosage adjustment, but does not address testing

**Red**

- FDA label cautions against use
- CMS decision against coverage
- Clincial practice guideline recommends against use of test
- Clinical practice guideline finds insufficient evidence and discourages use of test
- Systematic review recommends against use
- Systematic review finds insufficient evidence and discourages use
- Evidence available only from published studies without systematic reviews, clinical practice guidelines, FDA label or CMS labels coverage decision

*Can be reassigned to Green of Red of one or more conditions in these categories apply

http://www.cdc.gov/genomics/gtesting/tier.htm

# *MDCH-CDC Cancer Genomics Cooperative Agreements*

***Promoting Cancer Genomics Best Practices through Surveillance, Education, and Policy Change in the State of Michigan,* CDC-RFA-GD08-801**

- Purpose: move human genome applications into health practice to maximize health benefits and minimize harm through non-research activities
- Awarded from CDC Office of Public Health Genomics, 2008-2012
  - 3 year cooperative agreement (2008-2012) awarded to three grantees
  - Any organization eligible (except federal agency)
  - Translation of evidence-based recommendations for genetic tests into practice
    - 2005 USPSTF *BRCA* recommendations
    - EGAPP recommendations on Lynch syndrome
    - EGAPP recommendation on breast cancer gene expression profiling

***Enhancing Breast Cancer Genomics Best Practices and Policies in the State of Michigan,* CDC-RFA-DP11-1114**

- Purpose: develop or enhance activities related to breast cancer genomics
- Authorized from Affordable Care Act
- Awarded from CDC Division of Cancer Prevention & Control, 2011-2014
  - 3 year cooperative agreement (2011-2014) awarded to three grantees
  - State health departments and Tribal governments eligible
  - Promote use of BRCA1/2 clinical practices as recommended by USPSTF and NCCN
    - Must conduct programs in policy plus surveillance and/or health education
    - Cannot use funds for research, clinical practice or lobbying

# CDC Funding Announcement

## *Enhancing Cancer Genomic Best Practices through Education, Surveillance and Policy, 2014-2019*

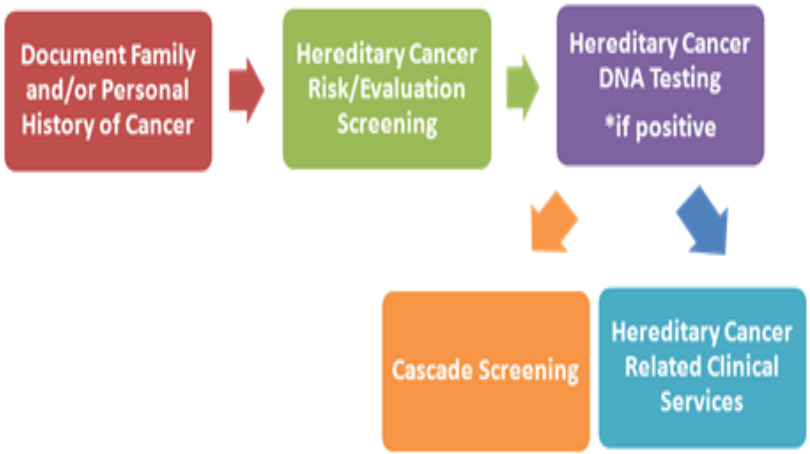



Figure 5: Cancer Genomics Best Practices

- **5 year** cooperative agreement awarded to four projects
  - Authorized from Affordable Care Act
  - State health departments and Tribal governments eligible
- **Purpose:** Enhance state health department's capacities to promote and apply evidence-based breast and ovarian cancer genomics guidelines in public health practice
  - Develop, enhance and evaluate education, surveillance and policy/systems change
  - Emphasis on partnerships
  - Focus on HBOC but may also include Lynch syndrome
  - May identify target populations disproportionately affected by HBOC and lack genetic services

# *MDCH Cancer Genomics Outcomes, 2014-2019*

- **Ultimate long term outcome**
  - Reduce incidence and mortality related to hereditary cancers, including breast, ovarian and colorectal cancer

- **Short- and intermediate term outcomes** (by 2019):
  - Increase knowledge among key clinical and policy stakeholders about cancer genetic best practices; improved access to and coverage of cancer genomics best practices **[Policy/system change]**
  - Improve ability to assess the burden of hereditary cancers and use of cancer genomics best practices; increased production and dissemination of periodic cancer surveillance reports. **[Surveillance]**
  - Increase knowledge of hereditary cancers and appropriate use of cancer genomics best practices among the public and health care providers. **[Education]**
  - Improve partnerships and coordination among key stakeholder groups regarding cancer genomics services and care. **[Partnerships]**

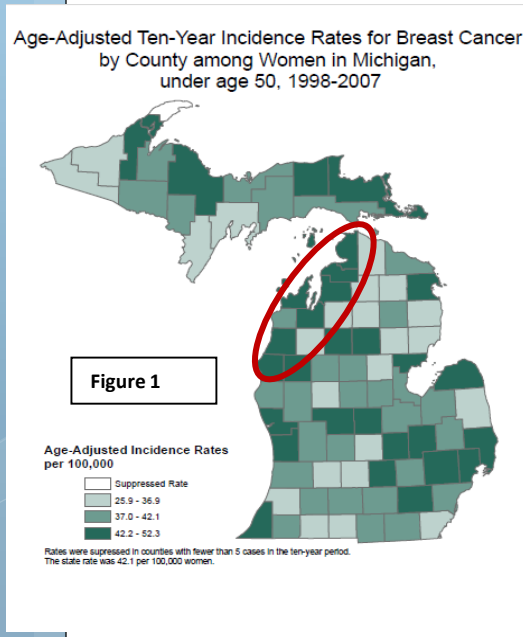



Figure 1

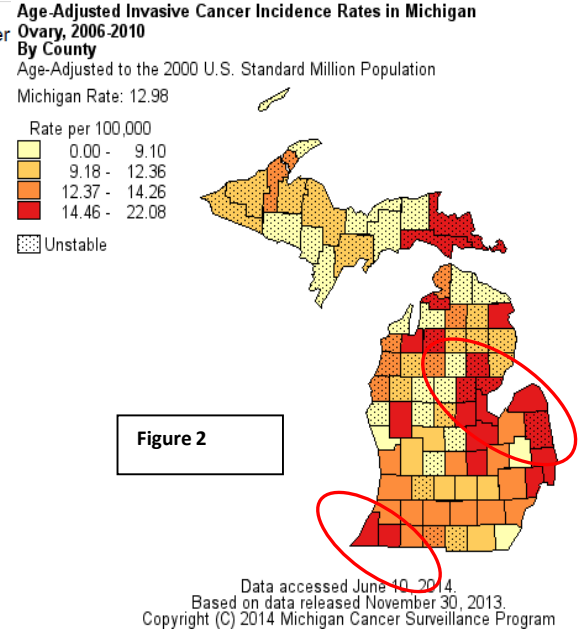



Figure 2

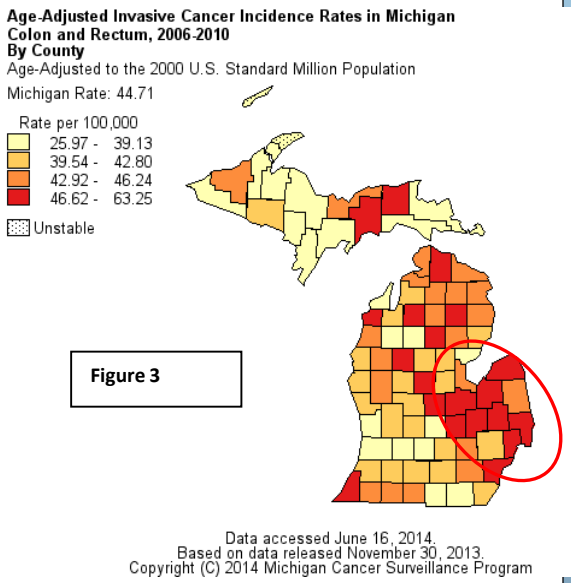



Figure 3

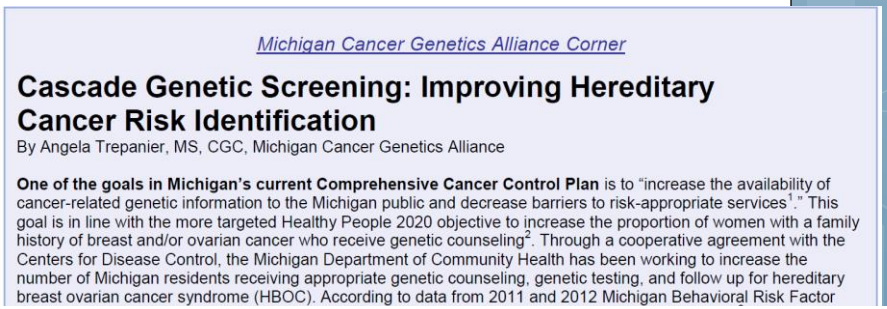
- High incidences are in geographic regions and counties that lack genetic services

# *Example of increasing knowledge of hereditary cancers among public and providers*

- Cascade screening!
- Individuals of a relative with a known deleterious mutation
  - 50% risk to inherit known deleterious mutation for first degree relatives
  - Single site testing is extremely informative and much less expensive

**http://kintalk.org/**





*Michigan Cancer Genetics Alliance Corner*

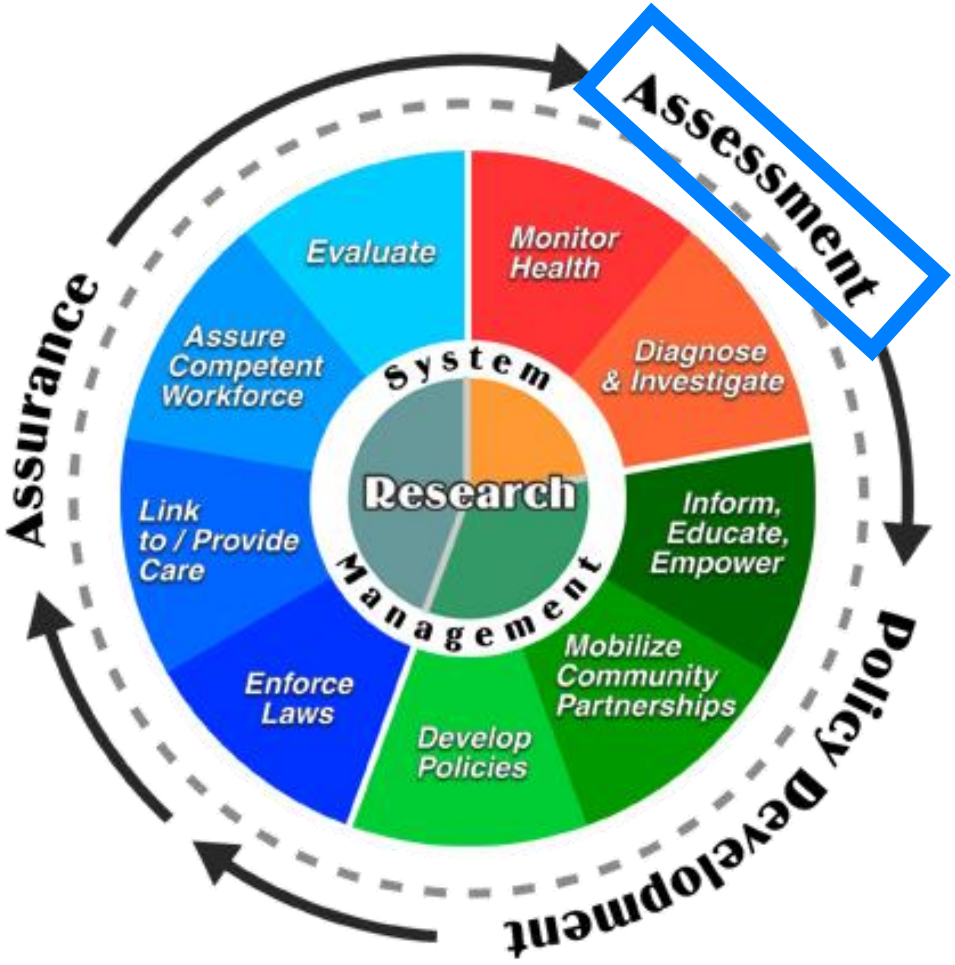
**Cascade Genetic Screening: Improving Hereditary Cancer Risk Identification**

By Angela Trepanier, MS, CGC, Michigan Cancer Genetics Alliance

**One of the goals in Michigan's current Comprehensive Cancer Control Plan** is to "increase the availability of cancer-related genetic information to the Michigan public and decrease barriers to risk-appropriate services[1]." This goal is in line with the more targeted Healthy People 2020 objective to increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling[2]. Through a cooperative agreement with the Centers for Disease Control, the Michigan Department of Community Health has been working to increase the number of Michigan residents receiving appropriate genetic counseling, genetic testing, and follow up for hereditary breast ovarian cancer syndrome (HBOC). According to data from 2011 and 2012 Michigan Behavioral Risk Factor

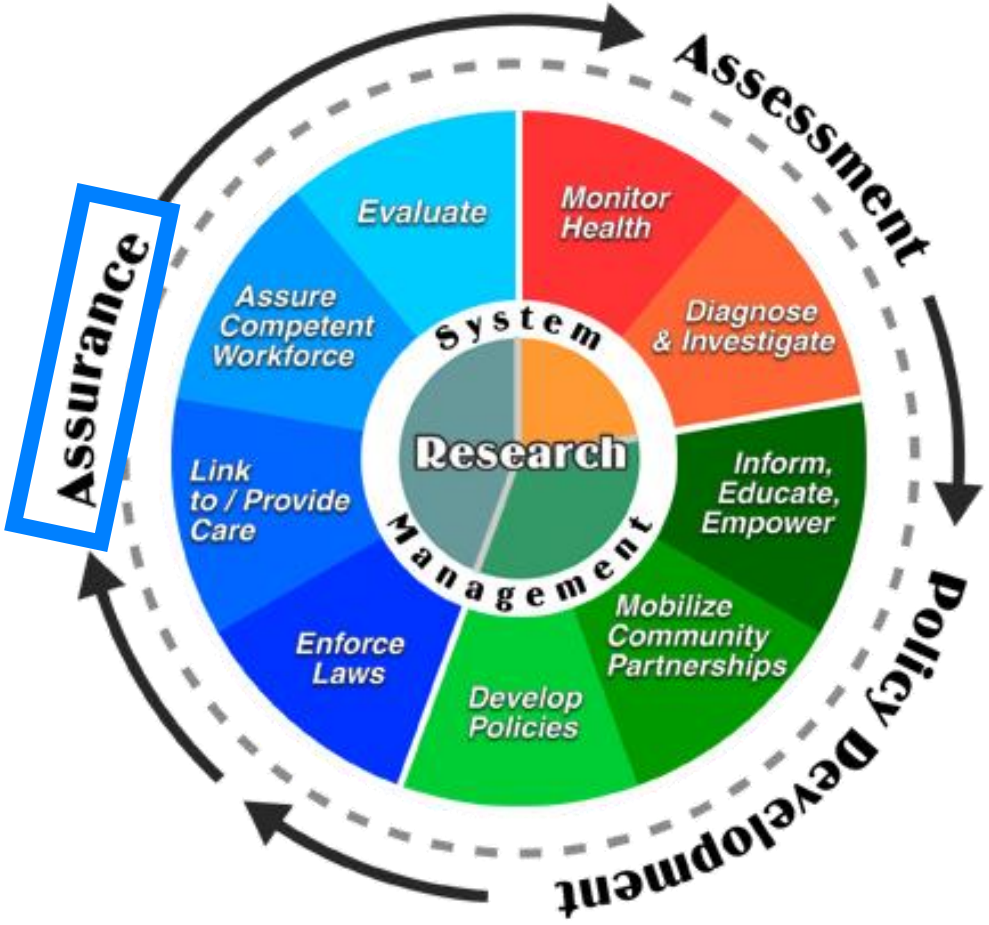
http://www.michigancancer.org/PDFs/Publications_Products/MCCUpdate/MCCUpdate2014/MCCUpdateJuly-Aug2014.pdf

# *Three Core Public Health Functions and Ten Essential Services*



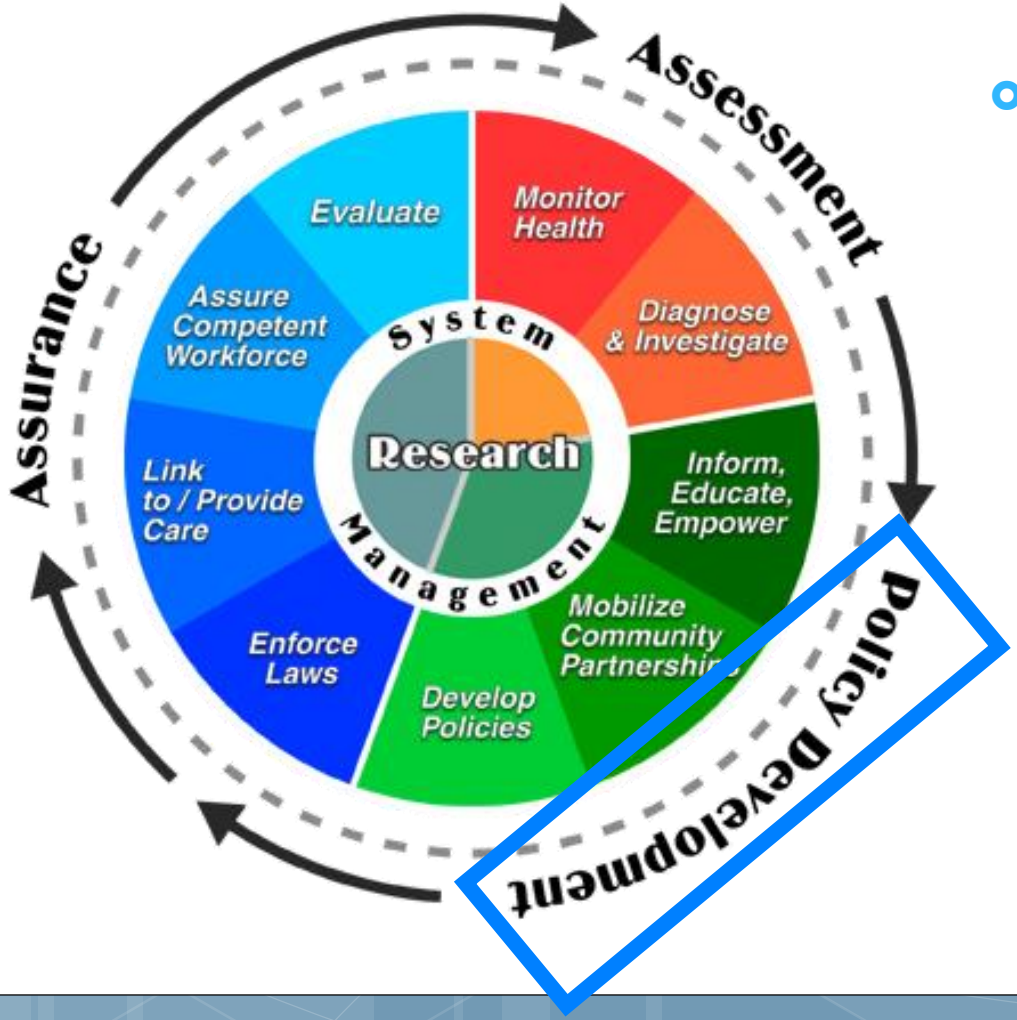

- **Assessment**: The regular systematic collection, assembly, analysis, and dissemination of information, including genetic epidemiologic information, on the health of the community

# *Three Core Public Health Functions and Ten Essential Services*




- **Assurance**: That genomic information is used appropriately and that genetic tests and services meet agreed upon goals for effectiveness, accessibility, and quality

# *Three Core Public Health Functions and Ten Essential Services*



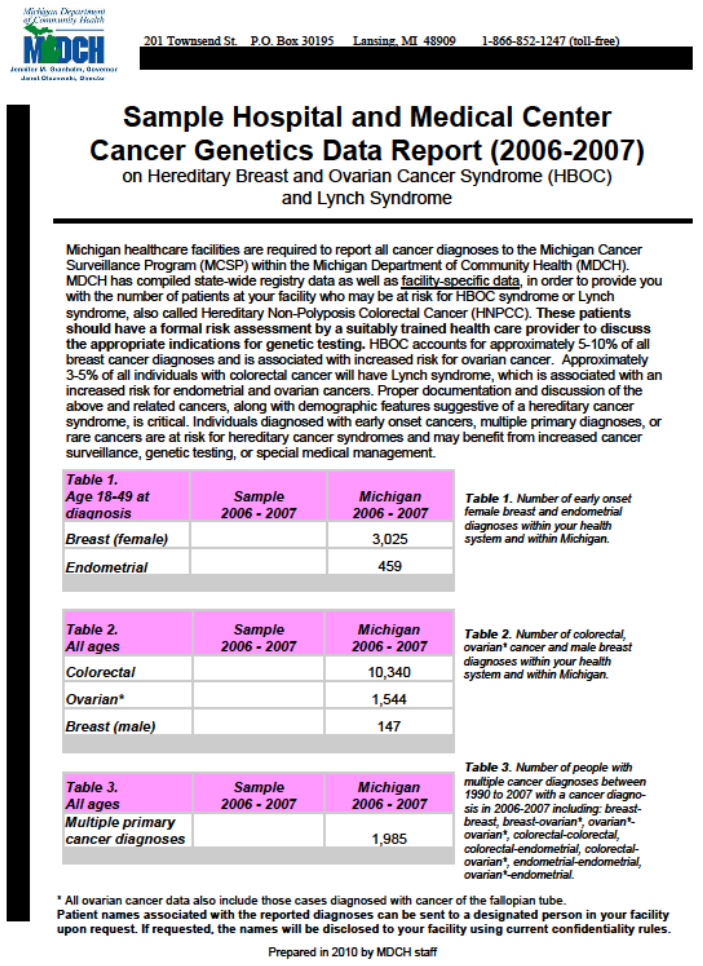

- **Policy Development**: The formulation of standards and guidelines, in collaboration with stakeholders, which promote the appropriate use of genomic information and the effectiveness, accessibility, and quality of genetic tests and services

# *Example of Cancer Genomics & Michigan Cancer Surveillance Program (MCSP) Activities*

- Utilized statewide cancer registry and mortality data to conduct cancer genomics surveillance since 2003
  - Existing data analyzed through ‘genomics lens’
  - Identify cases at high risk by age, gender, cancer type and with disparities based on race and county
    - Young women with breast cancer
    - Men with breast cancer
    - Women with ovarian cancer
    - **Multiple primary cancers** (i.e. breast-ovarian; colorectal-endometrial)
    - **Individuals with colorectal cancer**
  - Able to then utilize data for:
    - Health system and provider education
    - Patient education
    - Survey cancer patients and at-risk relatives
    - Monitor trends over time

# *Bidirectional Cancer Genomics Reporting using MCSP Data*

- Michigan identified over 15,000 cases of cancer relevant to HP 2020 cancer genomics objectives (2007-2008 MCSP data)
  - Numbers of breast (female at young age; male), ovarian, colorectal, endometrial and multiple primaries
- Informed key administrators at over 150 reporting institutions of their specific numbers of above cancer cases
- Included informational materials about hereditary breast and ovarian cancer and Lynch syndrome
  - Copies of evidence-based guidelines, Michigan cancer genetics directory, Michigan informed consent brochure, etc
  - Generate interests in Grand Rounds to learn more from cancer genetic professionals
- Connecticut reported back over 5,000 cases of cancer through a Healthy People 2020 Action Award (2008-2009 data)



Michigan Department of Community Health
MDCH
Jennifer M. Granholm, Governor
Janet Olszewski, Director

201 Townsend St. P.O. Box 30195 Lansing, MI 48909 1-866-852-1247 (toll-free)

**Sample Hospital and Medical Center**
**Cancer Genetics Data Report (2006-2007)**
on Hereditary Breast and Ovarian Cancer Syndrome (HBOC) and Lynch Syndrome

Michigan healthcare facilities are required to report all cancer diagnoses to the Michigan Cancer Surveillance Program (MCSP) within the Michigan Department of Community Health (MDCH). MDCH has compiled state-wide registry data as well as facility-specific data, in order to provide you with the number of patients at your facility who may be at risk for HBOC syndrome or Lynch syndrome, also called Hereditary Non-Polyposis Colorectal Cancer (HNPCC). **These patients should have a formal risk assessment by a suitably trained health care provider to discuss the appropriate indications for genetic testing.** HBOC accounts for approximately 5-10% of all breast cancer diagnoses and is associated with increased risk for ovarian cancer. Approximately 3-5% of all individuals with colorectal cancer will have Lynch syndrome, which is associated with an increased risk for endometrial and ovarian cancers. Proper documentation and discussion of the above and related cancers, along with demographic features suggestive of a hereditary cancer syndrome, is critical. Individuals diagnosed with early onset cancers, multiple primary diagnoses, or rare cancers are at risk for hereditary cancer syndromes and may benefit from increased cancer surveillance, genetic testing, or special medical management.

| Table 1. Age 18-49 at diagnosis | Sample 2006 - 2007 | Michigan 2006 - 2007 |
|---|---|---|
| Breast (female) | | 3,025 |
| Endometrial | | 459 |

*Table 1. Number of early onset female breast and endometrial diagnoses within your health system and within Michigan.*

| Table 2. All ages | Sample 2006 - 2007 | Michigan 2006 - 2007 |
|---|---|---|
| Colorectal | | 10,340 |
| Ovarian* | | 1,544 |
| Breast (male) | | 147 |

*Table 2. Number of colorectal, ovarian* cancer and male breast diagnoses within your health system and within Michigan.*

| Table 3. All ages | Sample 2006 - 2007 | Michigan 2006 - 2007 |
|---|---|---|
| Multiple primary cancer diagnoses | | 1,985 |

*Table 3. Number of people with multiple cancer diagnoses between 1990 to 2007 with a cancer diagnosis in 2006-2007 including: breast-breast, breast-ovarian*, ovarian*-ovarian*, colorectal-colorectal, colorectal-endometrial, colorectal-ovarian*, endometrial-endometrial, ovarian*-endometrial.*

* All ovarian cancer data also include those cases diagnosed with cancer of the fallopian tube.
**Patient names associated with the reported diagnoses can be sent to a designated person in your facility upon request. If requested, the names will be disclosed to your facility using current confidentiality rules.**

Prepared in 2010 by MDCH staff

# *Public Health Genomics Implementation to Save Lives: From National Vision to State Success*

https://www.youtube.com/watch?v=OfjkY1lLxbE&feature=youtu.be



- 2014 video created by CDC and Genetic Alliance
- Highlights Michigan as model for other states
- Importance of Partnerships!

# State and National Data on Lynch Syndrome Screening and Diagnosis

- No current source of national data
  - HP2020 objective is developmental
  - MSI only included in cancer registry reporting since 2010
    - Current pilot in select states regarding use of data element
- Michigan surveillance efforts for Lynch syndrome
  - Only 4 current health plans in Michigan have written policy aligned with EGAPP Lynch syndrome recommendations
  - Not feasible to utilize Medicaid claims data to determine CRC patients receiving Lynch syndrome testing
  - 2010 MiBRFS indicates nearly 80% of individual at risk for familial CRC syndrome report no knowledge of genetic test
    - Only 3% at risk for familial CRC syndrome had genetic test
  - Of 610 CRC charts reviewed from 2006-2010 diagnoses, less than 2% had Lynch syndrome screening
    - 6 had MSI testing; 11 had IHC; 0 had BRAF; 5 had MMR; 6 had genetic counseling (all among 119 cases aligned with NCCN guidelines)

Genet Med. 2013 Dec;15(12):933-40. doi: 10.1038/gim.2013.43. Epub 2013 May 2.

## Underutilization of Lynch syndrome screening in a multisite study of patients with colorectal cancer.

Cross DS[1], Rahm AK, Kauffman TL, Webster J, Le AQ, Spencer Feigelson H, Alexander G, Meier P, Onitilo AA, Pawloski PA, Williams AE, Honda S, Daida Y, McCarty CA, Goddard KA; CERGEN study team.

- National study utilized medical records from 7 HMO/health systems in Cancer Research Network to determine the availability of Lynch syndrome screening criteria and actual Lynch syndrome screening
  - Supports case for universal screening
  - Examined medical records of 1,188 patients diagnosed with metastatic colorectal cancer between 2004 and 2009
  - Found infrequent use (less than 5%) of Lynch syndrome screening (41/1,188)
  - Family history was available for 937 of the 1,188 patients (79%)
    - Sufficient to assess Lynch syndrome risk using family history-based criteria in 719 patients
    - 107 could not be evaluated due to missing information such as age of cancer onset
    - Only 11% percent of patients who met the Bethesda criteria and 25% of individuals who met the Amsterdam II criteria were screened for Lynch syndrome.

# *Columbus-area Lynch Syndrome Study (1999-2005)*

## 2.8% of CRC probands with deleterious mutations (n=44)

- Age at diagnosis – 51.4 (range 23-87)
- 50% diagnosed over age 50
- 25% did not meet either Amsterdam or Bethesda criteria
- Mutations
  - 20.5% *MLH1*
  - 52.3% *MSH2*
  - 13.6% *MSH6*
  - 13.6% *PMS2*

Hampel et al. *New Engl J Med* 2005; 352:1851
Hampel et al. *J Clin Oncol* 2008; 26:5783

# *Rationale for Lynch Syndrome Screening of Newly Diagnosed CRC*

- Common: ~ 3% of all CRC
- Age/screening criteria miss 25% or more
- Accurate methods (MSI/IHC) using easily accessible tumor tissue
- Benefits of medical intervention
  - Cascade testing of family members
  - Surveillance/prevention
  - CRC treatment decisions
- Evidence of cost-effectiveness

# *Universal LS Screening Implementation in US?*

GENETICS IN MEDICINE | SPECIAL ARTICLE

Implementing screening for Lynch syndrome among patients with newly diagnosed colorectal cancer: summary of a public health/clinical collaborative meeting

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*Genetics in Medicine* (2012) **14**, 152–162 | doi:10.1038/gim.0b013e31823375ea
Received 12 April 2011 | Accepted 17 August 2011 | Published online 27 October 2011

- Meeting held at CDC in September 2010 with multidisciplinary group
- Purpose to develop framework and partnerships to:
  - Implement clinical/public health approach to reduce morbidity and mortality associated with Lynch syndrome in the United States

# *Meeting Conclusions & Recommendations*

1. Genetic screening of all newly diagnosed CRC cases for LS (universal LS screening) can theoretically result in population health benefits, and feasibility has been demonstrated in research and clinical settings.
2. Utilizing a public health approach strongly integrated with all aspects of clinical care may provide the greatest opportunity for successful implementation on a regional or national scale.
3. There are several challenges and barriers to implementation of universal LS screening which need to be evaluated and addressed prior to consideration of large scale efforts at the state, regional or national level.
4. Education of clinicians, patients, families, healthcare system administrators, payers, and state and national public health entities and policy makers will be critical to any national effort.

Bellcross, Genet Med. 2012;14:152

5. National level conferences should be convened to allow further dialogue among key organizations, groups, and individuals regarding development of protocols, policies and guidelines addressing universal LS screening on a state and/or national level.

6. Serious consideration should be given to the paradigm of newborn screening as a model for implementing universal LS screening on a national level.

7. Carefully constructed pilot implementation projects and "real-world" studies are needed to demonstrate effectiveness and provide additional evidence of the feasibility and utility of population-level universal LS screening.

# Cost effectiveness Data

**Table 2** Cost-effectiveness ratios associated with Lynch syndrome testing strategies among new diagnosed patients colorectal cancer (CRC) and testing and surveillance for CRC among their first degree relatives

| Strategies | Description of testing strategy[a] | Incremental costs-effectiveness ratio of universal testing relative to no testing and relative to previous strategy, dollars per life-year saved | Incremental costs-effectiveness ratio of age-targeted testing relative to no testing and relative to previous strategy, dollars per life-year saved | Incremental costs-effectiveness ratio of universal testing relative to age-targeted testing and relative to previous strategy, dollars per life-year saved |
|---|---|---|---|---|
| 1 | IHC, *BRAF* testing and sequencing | $22,552 and $22,552 | $7,832 and $7,832 | $37,010 and $37,010 |
| 2 | IHC testing and sequencing | $23,321 and $273,915 | $7,944 and $60,569 | $38,411 and $429,973 |
| 3 | MSI testing and sequencing | $41,511 and $764,917 | $11,680 and $168,905 | $70,792 and $1,355,910 |
| 4 | Genetic sequencing for 4 genes | $142,289 and $737,025 | $44,902 and $252,643 | $237,278 and $1,192,575 |

[a]Sequencing includes detection of large deletions and rearrangements.

- Lowest cost testing strategy
  - IHC as a preliminary test for all newly diagnosed CRCs
    - Detects twice as many cases as using age-targeted testing
    - cost <or=$25,000 per life-year saved relative to no testing
    - Increasing number of relatives tested would improve cost-effectiveness

Mvundura M, et al. *Genet Med.* 2010;12:93-104

Journal of Genetic Counseling
September 2014

Date: 16 Sep 2014

# Creation of a Network to Promote Universal Screening for Lynch Syndrome: The Lynch Syndrome Screening Network

Sarah Mange, Cecelia Bellcross, Deborah Cragun, Deb Duquette, Lisa Gorman, Heather Hampel, Kory Jasperson

Lynch Syndrome Screening Network

- Created in September 2011 with one-time funding from CDC Office of Public Health Genomics:
  - Support for in-person meeting
  - Seed funding for database
- Founding Board of Directors from MDCH, Emory University, Huntsman Cancer Institute, The Ohio State University

# *LSSN Vision and Mission*

- **LSSN Vision:**
  - to reduce the cancer burden associated with Lynch syndrome.
- **LSSN Mission:**
  - to promote universal Lynch syndrome screening on all newly diagnosed colorectal and endometrial cancers; to facilitate the ability of institutions to implement appropriate screening by sharing resources, protocols and data through network collaboration; and to investigate universal screening for other Lynch syndrome related malignancies

# Members & Partners

**Full Membership**

- Institutions (hospitals, clinics, and academic medical centers) currently performing routine* tumor testing on colorectal cancers and/or endometrial cancers; AND
- Commitment to enter data (outlined by the research guidelines) regularly into the LSSN database for surveillance and/or research purposes; AND
- Institutional review board (IRB) approval (either obtained or in process) to enter data (outlined by the research guidelines) into the LSSN database; AND
- A genetic counselor or other qualified healthcare provider† trained in providing cancer genetic services is required to be at the institution; AND
- A genetic counselor or other qualified healthcare provider† must have access (either through clinical responsibilities and/or IRB approval) to both normal and abnormal routine* tumor testing results

**Affiliate Membership**

- Institutions (hospitals, clinics, and academic medical centers) performing routine testing*, but not meeting all criteria for full membership; OR
- Institutions interested in starting routine testing*

**Official Partners**

- Organizations interested in promoting routine testing* on all newly diagnosed colorectal and/or endometrial cancers that fall into the following categories:
  - Federal/state agencies
  - Professional societies
  - Patient support/advocacy groups
  - Laboratories (non-profit only) or companies

*Automatic tumor testing to evaluate for Lynch syndrome at the time of cancer diagnosis/surgery

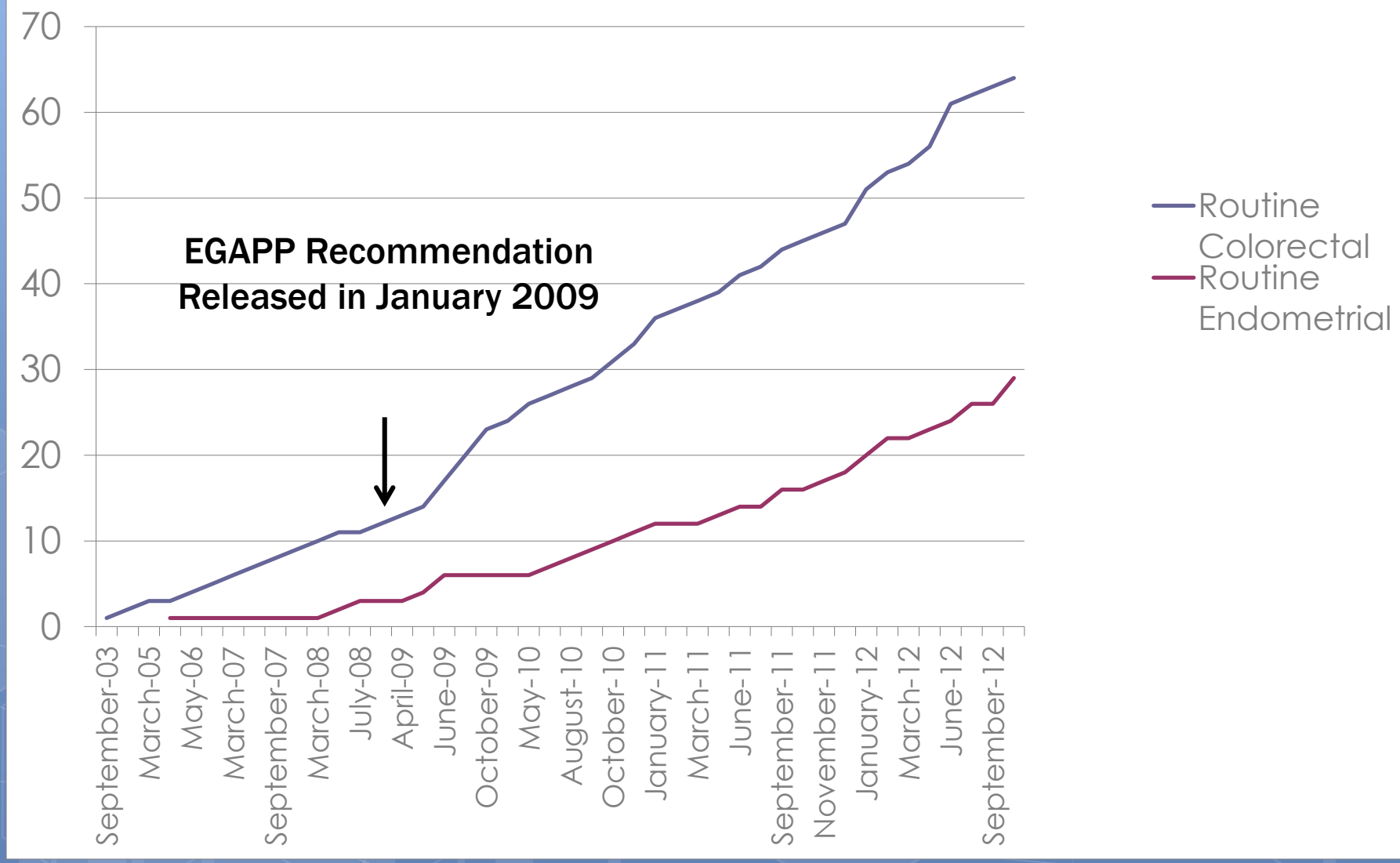
# Recruitment

- Institutions were invited to participate in the LSSN via select professional organizations involved in cancer genetics.
- Interested institutions completed an application that included information on:
  - existing screening protocols
  - plans for future implementation
  - screening for endometrial/other LS cancers
  - changes in number of cancers screened over time
  - willingness to contribute to a shared online database

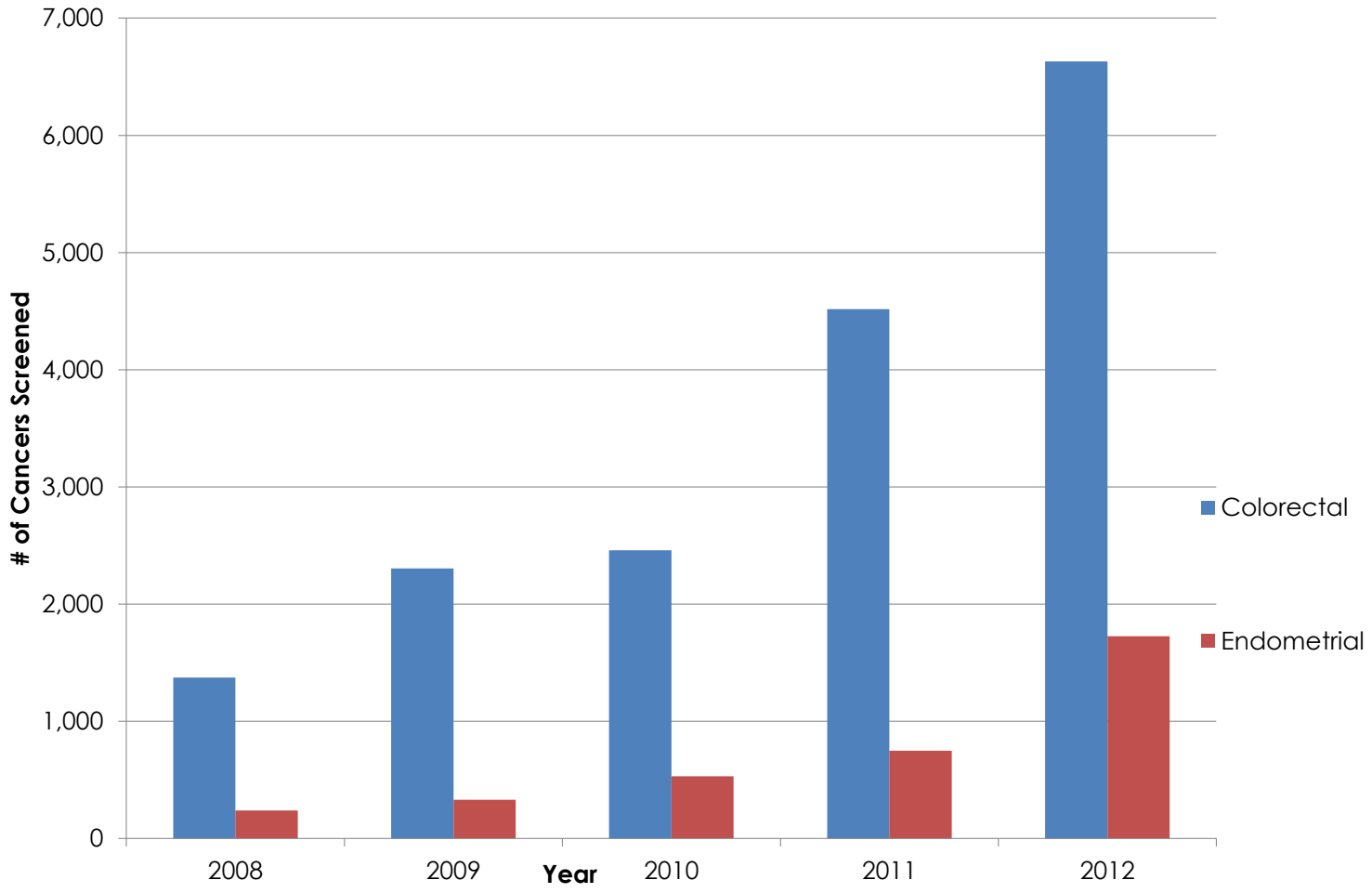
# Application Data

- 80 Institutions submitted applications to LSSN by 2014
  - 64 (80%) institutions currently providing routine tumor screening for Lynch syndrome on all or subset of colorectal cancers
  - 16 (20%) in the process of or planning to develop protocols for routine screening
  - 92% reported EGAPP justified, altered or supported LS screening protocols

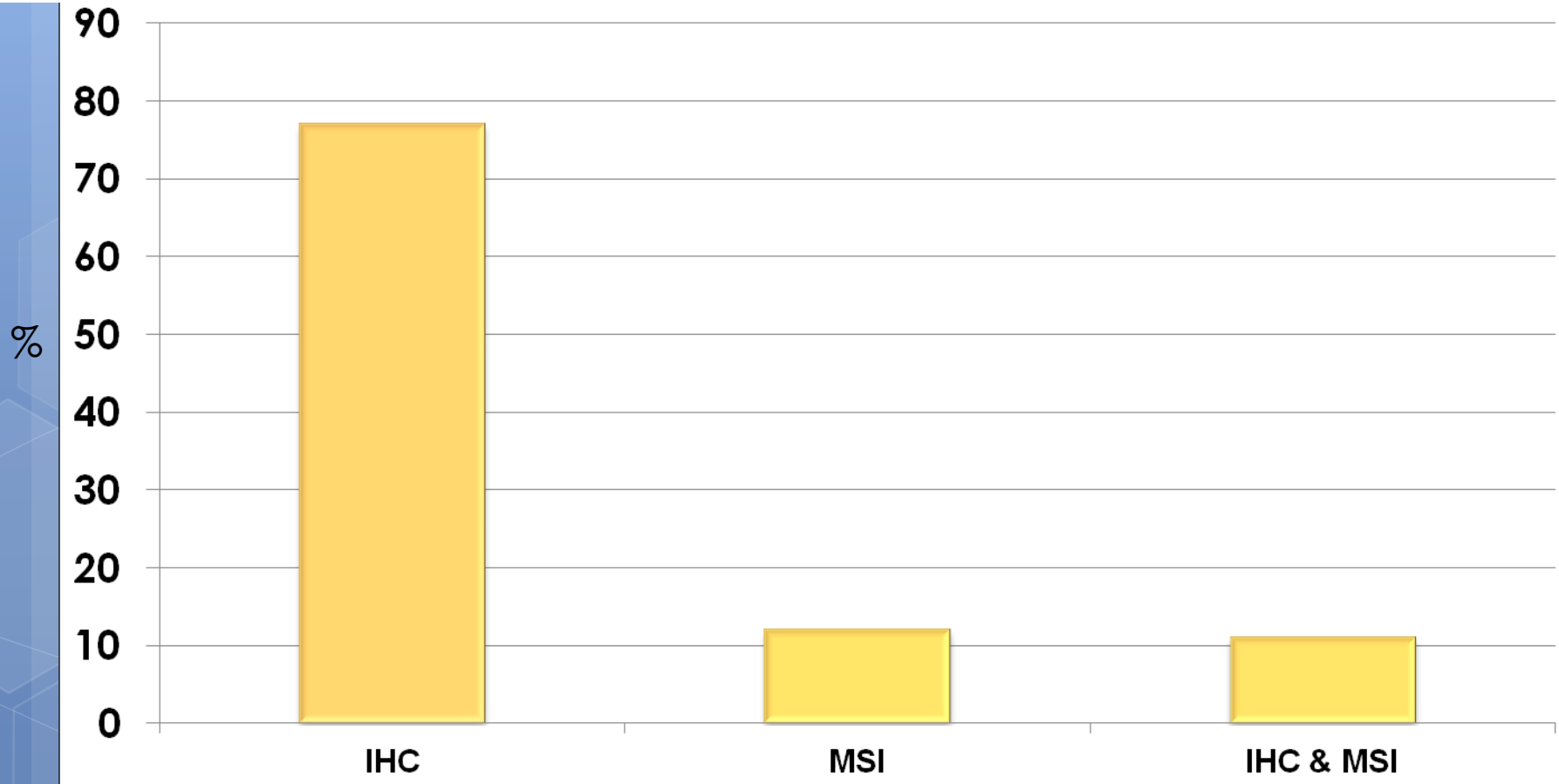
# Date Screening Initiated



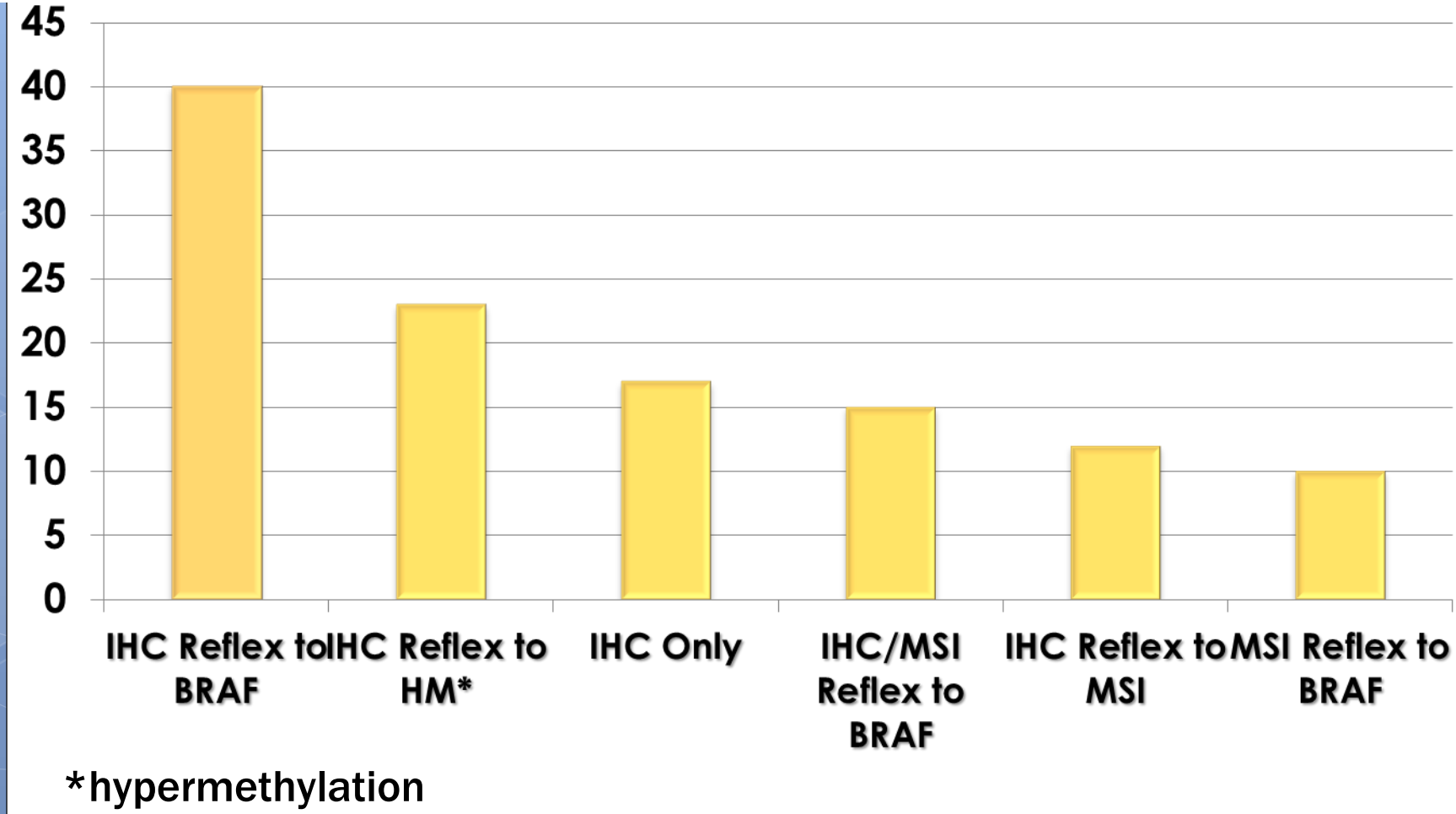
# Number of cancers screened for Lynch syndrome at time of pathological diagnosis, per year



# CRC Screening Protocols



# Screening Protocols




*hypermethylation

# LSSN Website
# www.lynchscreening.net

Lynch Syndrome Screening Network

LSSN Home | Development | Implementation | Resources | Database | Research | Membership | Events | Contact

## LSSN Home

***The vision of the LSSN is to reduce the cancer burden associated with Lynch syndrome***

LSSN Home
- News
  - March 22nd is Lynch Syndrome Day
  - New Strategies In Public Health Genomics
- History

Internet | Protected Mode: Off

# Implementation

There are multiple Lynch syndrome screening algorithms to choose from. These are briefly described below and detailed in their respective sections.

**MSI:** Microsatellite instability (MSI) testing can be performed on tumor tissue to gain more information about the likelihood of Lynch syndrome. Approximately 90% of colon tumors from individuals with Lynch syndrome demonstrate microsatellite instability (MSI), whereas only approximately 15% of sporadic colon tumors do.

**IHC:** Immunohistochemical (IHC) testing can be performed on tumor tissue to analyze mismatch repair protein function. Tumors from individuals with Lynch syndrome are likely to demonstrate loss of mismatch repair protein expression. The pattern of loss observed can provide information about which gene is not functioning properly. As a result, IHC can be helpful both in providing information about the likelihood of Lynch syndrome and in directing testing for a germline mutation to a specific gene.

Implementation

- Immunohistochemistry (IHC)
  - IHC Fact Sheets
  - IHC Procedures
  - IHC Results
- Microsatelite Instability (MSI)
  - MSI Fact Sheet
  - MSI Procedures
  - MSI Results
- Both MSI and IHC
  - MSI & IHC Fact Sheets
  - MSI & IHC Procedures
  - MSI & IHC Results

# LSSN Listserv

- Anyone from LSSN member or partner institution can be added to the listserv
  - Includes Karmanos!
- Very active listserv
- Excellent way for health professionals to receive variety of input quickly regarding:
  - Difficult dilemmas
  - Protocols
  - Ethical questions
  - Informed consent
  - Billing issues

- Example of recent inquiry from health professional at member institution
  - Method of informed consent (if any) used prior to universal screening?
    - 45 LSSN institutions replied within 3 days of inquiry
      - 73.33% no informed consent
      - 24.44% informed consent via information sheet provided in advance
      - 0% verbal consent
      - 2.22% written consent

Lynch Syndrome Screening Network

LSSN Home | Development | Implementation | Resources | Database | Research | Membership | Events | Contact

## Database

**Who can use the database?**

Institutions that have full membership will have access to aggregate database information. Institutions who participate in the database will have open access to their own data for internal purposes.

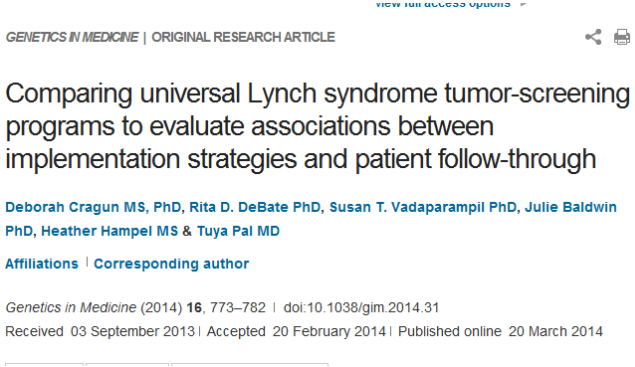
Link to Password Protected Database

Database

- Instructions
- Outcomes
- Database Elements

www.lynchscreening.net

# *Example of LSSN Implementation Study*



GENETICS IN MEDICINE | ORIGINAL RESEARCH ARTICLE

Comparing universal Lynch syndrome tumor-screening programs to evaluate associations between implementation strategies and patient follow-through

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*Genetics in Medicine* (2014) **16**, 773–782 | doi:10.1038/gim.2014.31
Received 03 September 2013 | Accepted 20 February 2014 | Published online 20 March 2014

- Multiple-case study of 15 LSSN institutions
- Categorized as Low-PF (≤25% underwent germ-line testing), Medium-PF (26-55%), or High-PF (>56%)
- Five High-PF institutions:
  - disclosure of screen-positive results to patients by genetic counselors
  - genetic counselors either facilitate physician referrals to genetics professionals or eliminate the need for referrals
  - automatic reflex testing
  - ability to contact screen-positive patients was not a barrier

# Figure 1. Patient Reach Scores and Factors associated with Patient Reach

**H-R**: 7 =>85%; 6 = 71-85%; 5 = 56-70%

**M-R**: 4 = 41-55%; 3 = 26-40%

**L-R**: 2 = 11-25%; 1 = <10%

| Institution | Patient reach score | Implementation challenges> facilitators | **Automatic** reflex testing (i.e., BRAF) | **Genetics** receives copy of positive screens | **Genetics** discloses result to patient | Difficulty contacting patients | Physician **refers** follow-up testing |
|---|---|---|---|---|---|---|---|
| H1 | 6 | | X | X | X | | |
| H2 | 5.5 | | X | X | X | | |
| H3 | 5 | | X | X | X | | |
| H4 | 5 | | X | X | X | | |
| H5 | 5 | X | X | X | X | | |
| M1 | 4 | | | X | X | X | |
| M2 | 3.5 | | X | X | | X | X |
| M3 | 3 | | | X | X | X | |
| M4 | 3 | | X | X | | | X |
| M5 | 2.5 | | X | X | | | X |
| L1 | 1.5 | X | | X | | | X |
| L2 | 1 | X | | X | | | X |
| L3 | 1 | X | X | X | | | X |
| L4 | 1 | | X | | | | X |
| L5 | 1 | | | | | | X |

# *Today's Reality: Many Unanswered Questions*

- Of the ~400 people in US who will be diagnosed with CRC today, ~12 of these people will have Lynch syndrome
  - How many of these 400 people are being screened for Lynch syndrome?
  - How many of the 12 are being diagnosed with Lynch syndrome?
  - How many of their relatives are being screened?
  - How many lives saved by Lynch syndrome diagnosis?

# *Thank you!*

Funding for these projects were made possible by multiple cooperative agreements from the Centers for Disease Control and Prevention. The contents are solely the responsibility of the author and does not necessarily represent the official views of CDC.